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TITLE: Estrogens, Genetic Polymorphisms and Breast Cancer Risk

PRINCIPAL INVESTIGATOR: Michael N. Okobia, M.D.
Clareann H. Bunker, Ph.D.
Lewis Kuller, M.D., Dr. PH
Robert E. Ferrell, Ph.D.
Stanley N.C. Anyanwu, FWACS
Emmanuel R. Ezeome, FWACS
Emmanuel E.O. Uche, M.D., Ph.D.

CONTRACTING ORGANIZATION: University of Pittsburgh
Pittsburgh, Pennsylvania 15260

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**6. AUTHOR(S)**
Michael N. Okobia, M.D., Clareann H. Bunker, Ph.D., Lewis Kuller, M.D., Dr. PH, Robert E. Ferrell, Ph.D., Stanley N.C. Anyanwu, FWACS, Emmanuel R. Ezeome, FWACS, Emmanuel E.O. Uche, M.D., Ph.D.

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
University of Pittsburgh
Pittsburgh, Pennsylvania 15260

E-Mail: michaelokobia@yahoo.com

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**13. ABSTRACT (Maximum 200 Words)**

This study is aimed at evaluating the role of polymorphisms in the genes encoding enzymes responsible for the biosynthesis and degradation of estrogens and its metabolites in susceptibility to breast cancer in Nigerian women. A case-control study is being undertaken to investigate the exposure level to estrogen and its metabolites in these women by examining the genotype frequencies of the genes encoding aromatase, estrogen hydroxylase and catechol-O-methyltransferase, the three major enzyme systems involved in the biosynthesis and degradation of estrogen and its metabolites. Polymorphisms in these genes have been reported to influence breast cancer risk in African American women. Since Nigerian women share common genetic ancestry with African American women, it is biologically plausible to speculate that similar genetic factors may be acting to determine breast cancer risk in both populations. The first 20 months of the study (i.e., August 2002 and April 2004) was spent in recruiting 500 study participants from Nigeria and transferring study documents and biological samples from Nigeria to the University of Pittsburgh. Data entry was accomplished in May and June 2004 and descriptive data analysis is currently on going. DNA extraction is underway. Genotyping will be completed in the final year.

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## Table of Contents

## Annual Summary Report for Award Number DAMD17-02-1-0551

## Introduction

This annual summary report is for the breast cancer study titled "Estrogens, Genetic Polymorphisms and Breast Cancer Risk" (Award Number: DAMD17-02-1-0551). The study was awarded to University of Pittsburgh Cancer Institute (UPCI) in Fiscal Year 2001 Department of Defense Breast Cancer Research Program (BCRP) of the U.S. Army Medical Research and Materiel Command's Office of the congressionally Directed Medical Research Programs (CDMRP). The grant category was post-doctoral training with Michael N. Okobia as the principal investigator and Clareann H. Bunker, Ph.D an Associate Professor in the Department of Epidemiology, University of Pittsburgh as co-Principal Investigator. Other Co-Investigators from University of Pittsburgh include Lewis H. Kuller, MD, Dr.P.H.; and Robert E. Ferrell, Ph.D. The Nigerian Co-Investigators are Stanley N.C. Anyanwu, MBBS, FWACS, FMCS; Emmanuel R. Ezeome, MBBS, FWACS, and Emmanuel E.O. Uche, MD, SCGS, Ph.D, FWACS.

**Body**

This collaborative study between investigators at the University of Pittsburgh and their Nigerian colleagues drawn from four University Teaching Hospitals in Nigeria (University of Benin Teaching Hospital, University of Nigeria Teaching Hospital, Nnamdi Azikiwe University Teaching Hospital and University of Port Harcourt Teaching Hospital) was designed to evaluate the presence of polymorphisms in three major genes involved in estrogen metabolism and the role of any detected polymorphisms in these genes in breast cancer susceptibility among Nigerian women. A case-control design recruiting 250 women with proven breast cancer and 250 age-matched controls without breast cancer was adopted for the study. The study was designed to last for three years, from August 2002 to July 2005. By 30 June 2003, 212 study participants comprising 141 cases and 71 controls had been recruited.

**Key Research Accomplishments**

Within the period under review (1 July 2003 – 30 June 2004), an additional 288 study participants comprising 109 cases and 179 controls were recruited into the study bringing the total recruitment to the target sample size of 250 cases and 250 controls. Details of monthly recruitment from the four Nigerian study sites are shown in the Table I below. All research records and biological samples for all study participants have been transferred from Nigeria to the University of Pittsburgh in April 2004. Since arriving University of Pittsburgh in May 2004, data entry has been completed and descriptive analysis of the data is on going. We have just completed data entry and descriptive analysis is currently going on. In addition, the necessary classes in Biohazards related to laboratory work in preparation for DNA extraction and genotyping of the samples have been completed. DNA extraction has just commenced and this phase of DNA extraction and genotyping is expected to complete by December 2004.

Table I: Details of Monthly recruitment of Study Participants from the Nigerian Study Sites (July 2003 – March 2004)

| | University of Benin Teaching Hospital (UBTH) | | University of Nigeria Teaching Hospital (UNTH) | | Nnamdi Azikiwe University Teaching Hospital (NAUTH) | | University of Port Harcourt Teaching Hospital (UPTH) | |
|---|---|---|---|---|---|---|---|---|
| | Cases | Controls | Cases | Controls | Cases | Controls | Cases | Controls |
| July 2003 | 2 | 3 | 1 | 11 | 0 | 4 | 4 | 1 |
| August 2003 | 4 | 0 | 9 | 4 | 4 | 5 | 0 | 4 |
| September 2003 | 2 | 14 | 3 | 4 | 0 | 2 | 5 | 2 |
| October 2003 | 2 | 9 | 8 | 4 | 3 | 1 | 6 | 0 |
| November 2003 | 0 | 5 | 6 | 8 | 6 | 1 | 0 | 8 |
| December 2003 | 3 | 0 | 3 | 5 | 0 | 6 | 0 | 6 |
| January 2004 | 4 | 0 | 2 | 3 | 5 | 4 | 0 | 4 |
| February 2004 | 2 | 0 | 2 | 12 | 8 | 10 | 4 | 0 |
| March 2004 | 2 | 0 | 3 | 26 | 6 | 20 | 0 | 3 |
| Total | 21 | 31 | 37 | 67 | 32 | 53 | 19 | 28 |

Total Number of Cases = 109
Total Number of Controls = 179
Grand Total = 288

**Reportable Outcomes**

There are yet no reportable outcomes in this study. However preliminary data analysis of descriptive epidemiology evaluating the role of various risk factors in breast cancer risk in the study population is currently on going.

**Conclusions**

In the past one year since the last annual summary report, the study has progressed steadily with recruitment of study participants completed by the end of March 2004. However, there were occasional interruptions of recruitment of study participants occasioned by industrial actions in the Petroleum industry in Nigeria during this period. All the study data and biological specimens have also been transferred to the University of Pittsburgh. Data entry has also been completed and descriptive analysis of the data is on going. Laboratory work has just commenced and hopefully DNA extraction and genotyping will be completed by the end of December 2004. Within this period, it is also hoped that data analysis on descriptive epidemiology of risk factors for breast cancer in the study population will be completed. The last six months of the study (January to June 2005) will be spent of writing final report for the study.

**References** (none)

**Appendices** (none)